**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION**
**DECISION SUMMARY**
**ASSAY ONLY TEMPLATE**

**A. 510(k) Number:**

K501478

**B. Purpose for Submission:**

To add Rifampin to the MicroScan® Synergies plus™ Gram-Positive MIC/Combo Panels

**C. Measurand:**

Rifampin at 0.25 - 8 µg/mL

**D. Type of Test:**

Quantitative and Qualitative growth based detection algorithm using optics light detection

**E. Applicant:**

Dade Behring Inc,
MicroScan®

**F. Proprietary and Established Names:**

MicroScan® Synergies plus™ Gram-Positive MIC/Combo Panels

**G. Regulatory Information:**

1. Regulation section:

   866.1645 - Fully automated short-term incubation cycle antimicrobial susceptibility system
   866.1640 - Antimicrobial Susceptibility Test Powder

2. Classification:

   Class II

3. Product code:
   LON – Automated AST system short incubation

LRG-Instrument for Auto Reader & Interpretation of Overnight Antimicrobial Susceptibility Systems
JWY - Manual Antimicrobial Susceptibility Test Systems
LTT – Panels, Test, Susceptibility, Antimicrobial

4. Panel:
   83 Microbiology

## H. Intended Use:

1. Intended use(s):

   For use with MicroScan® Synergies plus™ Panels read on the WalkAway® -SI System (including upgraded WalkAway® -40 or WalkAway® -96 to meet WalkAway® SI equivalence). MicroScan® panels are designed for use in determining quantitative and/or qualitative antimicrobial agent susceptibility and/or identification to the species level of colonies, grown on solid media, of rapidly growing aerobic and facultative anaerobic gram-positive cocci and Listeria.

2. Indication(s) for use:
   The testing of rifampin at concentrations of 0.25 – 8 µg/mL to the gram-positive test panel for testing *Staphylococcus* spp. at 4.5-16 hours or 16-20 hours for a overnight reading.

3. Special conditions for use statement(s):
   - Turbidity method of inoculum preparation only.
   - For prescription use only.

4. Special instrument requirements:

   Not Applicable

## I. Device Description:

Each panel contains two control wells: a negative control well, and a growth control well (contains test medium without antibiotic). Antibiotics are diluted in water, buffer, or minute concentrations of broth to selected concentrations prior to dehydration of the panels. The panel is rehydrated and inoculated at the same time with 0.1 ml of suspension prepared by the turbidity method (inoculum prepared in 0.4% saline with Pluroinc®, then 0.1ml transferred to 25ml of inoculum Synergies plus Pos Broth with Pluronic®) for a final inoculum concentration of 3-7 X $10^5$ CFU/ml. Panels are incubated in a Walk-Away® System and read periodically starting at 4.5 hours until sufficient growth to determine the MIC. Alternately the panels may be incubated at $35^o$ C in a non-$CO_2$ for 16-24 hours and read by visual observation of growth.

**J. Substantial Equivalence Information:**

1. Predicate device name(s):

   MicroScan® Dried Gram-Positive and Gram-Negative MIC/Combo Panels

2. Predicate 510(k) number(s):

   k862140
   k020185

3. Comparison with predicate:

| Similarities | | |
|---|---|---|
| **Item** | **Device** | **Predicate** |
| Intended use | MicroScan® panels are designed for use in determining quantitative and/or qualitative antimicrobial agent susceptibility and/or identification to the species level of colonies, grown on solid media, of rapidly growing aerobic and facultative anaerobic organisms | Same |
| Specimen | Isolated colonies from culture used | Same |
| Inoculum | Inoculum density to 0.5 McFarland standard | Same |
| Incubation | <16 hours<br>16 – 24 hours | Same |
| Results | Quantitative with qualitative interpretations | Same |
| Technology | Growth based | Same |

| Differences | | |
|---|---|---|
| **Item** | **Device** | **Predicate** |
| Panels | Dried rifampin in water | Dried clindamycin or gentamicin in broth |
| Reading | Uses both a ≤ 16 hour read and overnight read method in the same system | Overnight system uses only the overnight reading method and <16 hour instruments use only the <16 hour read method. |
| Inoculum preparation | Turbidity method of inoculation only. | Inoculum prepared using either the Turbidity method or Prompt® system |
| Instrument | WalkAway® -SI System or equivalent | autoScan® -4 or WalkAway® |
| Antibiotic | Rifampin at 0.25 – 8 µg/mL | Different concentrations depending on the antibiotic |

**K. Standard/Guidance Document Referenced (if applicable):**

Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA"; Clinical and Laboratory Standards Institute (CLSI) M7 (M100-S15) "Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard".

**L. Test Principle:**

The WalkAway® SI uses a Colorimetric Optics System consisting of a color wheel/lamp assembly and a Photosensor. There is an initial read at 2.5 hours with a possible final read at 4.5, 5.5, 6.5, 8, 12, 16 or18 hours (overnight instrument readings, manual readings) depending on the growth rate of the organism being tested. The time of final read is dependent on the user customization, the growth rate of the organism, and the sensitivity of the automatic reader since cell densities below 2 x $10^7$ cells/ml are not detected.

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**M. Performance Characteristics (if/when applicable):**

1. Analytical performance:

   a. *Precision/Reproducibility:*
   Reproducibility was demonstrated using 270 isolates, tested at 3 sites on 3 separate days in triplicate. The study included the testing on the WalkAway® SI read at <16 hours, WalkAway® 16-18 hour readings and manual readings at 16-20 hours incubation. The WalkAway® SI had 3 results that were not readable at <16 hours. All reading methods were overall reproducible at >95%, except for the <16 hour readings. The result from one site was lower than expected providing results just below the acceptable criteria.

   b. *Linearity/assay reportable range:*

   Not Applicable

   c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

   The recommended QC isolate was tested a sufficient number of times with acceptable results on all testing days with the reference method. All Synergy Plus panels, which are configured to produce readings at <16 hours, provided QC results in the 4.5-16 hour window. Quality control results demonstrated the ability of the different reading parameters (manual and instrument) to produce acceptable results. The following table provides the frequency of the results in each concentration tested with the expected range stated.

| | | | Results | | |
|---|---|---|---|---|---|
| Organism | Conc in µg/mL | # reference | MicroScan® | | |
| | | | Manual overnight | Instrument overnight | <16 hours Instrument |
| *E. faecalis* ATCC 29212 Range 0.5 – 4 µg/mL | <=0.25 | | | | |
| | 0.5 | 29 | 22 | 24 | 24 |
| | 1 | 1 | 8 | 6 | 6 |
| | 2 | | | | |
| | 4 | | | | |
| | 8 | | | | |
| | >8 | | | | |
| | | | | | |
| *S. aureus* ATCC 29213 Range <=0.25 µg/mL | <=0.25 | 30 | 29 | 29 | 30 |
| | 0.5 | | 1 | 1 | |
| | 1 | | | | |
| | 2 | | | | |
| | 4 | | | | |
| | 8 | | | | |
| | >8 | | | | |

No trending was observed. The modes for the reference method and the test device are the same.

Inoculum density control: A turbidity meter was used for the turbidity inoculation method. Turbidity inoculum verification provided.

*d. Detection limit:*

Not Applicable

*e. Analytical specificity:*

Not Applicable

*f. Assay cut-off:*

Not Applicable

2. Comparison studies:

*a. Method comparison with predicate device:*
Clinical testing was conducted at 3 sites using fresh isolates supplemented with stock isolates. A total of 301 gram-positive isolates were tested of which 263 were fresh isolates and 38 were stock isolates. There were 75 challenge

isolates tested at one site and compared to the reference broth dilution result mode that was determined by previous testing of each isolate multiple times in the recommended reference panel. The Synergies plus™ readings were obtained at times between 4.5 and 16 hours of incubation for > 95% of the results. An additional comparison was done with readings on the instrument after overnight incubation and also read manually when incubated 16- 18 hours. Performance by these alternate reading methods was also acceptable with no apparent differences or trends.

The recommended CLSI reference method was followed with the exception of the use of a small amount (0.1%) Pluronic® in the final inoculum. A validation of the use of Pluronic® in the frozen reference panels was conducted. Similar calculations for the different reading methods were performed with very little difference. QC was also performed with minimal difference apparent in the results.

The chart below demonstrates the performance of all three reading methods (Synergies plus™ readings at <16 hours, overnight on the WalkAway® and manually read at 18 hours using the touchScan®-SR) when compared to the reference method.

| Reading Methods | total | EA | %EA | Total evaluable | EA of evaluable | %EA | CA | %CA | #R | min | maj | vmj |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **<16 hours** | 374 | 370 | 98.9 | 18 | 18 | 100.0 | 365 | 97.6 | 22 | 7 | 2 | 0 |
| **Overnight Instrument** | 376 | 375 | 99.7 | 19 | 19 | 100.0 | 367 | 97.6 | 22 | 8 | 1 | 0 |
| **Overnight Manual** | 376 | 374 | 99.5 | 19 | 17 | 89.5 | 362 | 96.3 | 22 | 13 | 1 | 0 |

**EA-**Essential Agreement
**CA**-Category Agreement
**R**-resistant isolates
**maj**-major discrepancies
**vmj**-very major discrepancies
**min-** minor discrepancies

Evaluable results are those that fall within the test range of the reference method and could also be on-scale with the new device if within the plus/minus one dilution variability. EA is when there is agreement between the reference method and the MicroScanMicroScan® Synergies plus® within plus or minus one serial two-fold dilution of antibiotic. CA is when the interpretation of the reference method agrees exactly with the interpretation of the MicroScan® Synergies plus result.

*b. Matrix comparison:*

Not Applicable

3. Clinical studies:

   *a. Clinical Sensitivity:*

   Not Applicable

   *b. Clinical specificity:*

   Not Applicable

   c. Other clinical supportive data (when a. and b. are not applicable):

   Not Applicable

4. Clinical cut-off:

   Not Applicable

5. Expected values/Reference range:

   *Staphylococcus* spp. interpretive criteria:

   <=1 (Susceptible), 2 (Intermediate), >=4 (Resistant)

   The expected value range, interpretive criteria and QC values are included in the package insert.

**N. Proposed Labeling:**

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

**O. Conclusion:**

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.